^{72}Se/^{72}As. An important research strand is also devoted to the alternative (in opposition to the classical reactor route via ^{99}Mo generator) accelerator production method of the most popular nuclear medicine radioisotope, ^{99m}Tc. The research on accelerator produced medical radioisotopes based on the HIL cyclotrons is conducted within a large collaboration, involving the Heavy Ion Laboratory, the University of Silesia, the Institute of Nuclear Chemistry and Technology (INCT), POLATOM at the National Centre for Nuclear Research, the Centre of Biological and Chemical Research of the University of Warsaw and the Institute of Nuclear Physics in Kraków. After target preparation and irradiation the properties of the produced radioisotopes are first investigated at HIL via gamma-ray spectroscopy techniques and subsequently transported to INCT or POLATOM for further chemical investigations. Table below shows some of the obtained results.
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Keywords: medical radioisotopes

TABLE I
Investigated radioisotopes

Isotope	Target	Energy [MeV]	TTY* [MBq/μAh]	Comment
^{211}At	^{209}Bi	α 29	37(6)	(a)
^{72}Se	$^{nat}GeO_2$	α 30	0.19(3)	(a)
^{72}As			2.7(1)	
^{43}Sc	$^{nat}CaCO_3$	α 20	84(4)	(b)
^{44gd}Sc	$^{42}CaCO_3$ (95.9%)	α 29	44(7)	(b)
^{44m}Sc			4.7(8)	
^{99m}Tc	^{100}Mo (99.815%)	p 16 p 25	372(25) 806(133)	-
^{99}Mo		p 16 p 25	2.4(6) 18(7)	-

* Thick Target Yield
(a) From K. Szkliniarz et al. Acta Phys. Pol. A127, 1471
(b) From K. Szkliniarz et al. submitted for publication

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Comparison of the various paths of ^{44}Sc isomeric pair production

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The ^{44}Sc isomeric pair has attracted a lot of attention in recent years as a candidate for various applications in nuclear medicine [1-6]. Colloquially speaking, this pair can be considered as an "ARRONAX" isotope, with applications in Three Photon PET techniques already suggested in 2007[1], and the 58 h high spin (6+) isomeric state, decaying by 99% IT to the 4 h (2+) ground state, as an *in vivo* generator discussed recently in Refs [4-6]. This ground state undergoes in turn predominantly the β^+ decay to the 1157 keV excited state in ^{44}Ca. The previously investigated production of ^{44m}Sc using the deuteron beams is extended to alpha particle projectiles in the present work. It is well known that due to its larger mass and higher bombarding energy, the alpha particle transfers to the compound nucleus a larger angular momentum than lighter projectiles. Although the production efficiency (Thick Target Yield) of the high spin isomer is not much augmented with this projectile, the isomeric ratio is substantially increased (from 2.2% up to 10.9%, see table below) which should allow this isomer to be produced with a much lower contribution of the directly formed ground state decay; as discussed in previous references, this is very important for synthesis of the *in vivo* ^{44}Sc generator.

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Keywords:
medical radioisotopes

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TABLE I
Thick Target Yield of ^{44gd}Sc ($^{42}CaCO_3$ or ^{41}KCl targets) and the ratio of TTY of ^{44m}Sc/^{44gd}Sc for p, d and α projectiles estimated from Refs. 2-5 and the present work.

Projectile	p	d	α	α	α
Projectile energy (MeV)	15.6	14.9	20	29	50
Target	^{44}Ca (98%)	^{44}Ca (96.9%)	^{41}K (95.4%)	^{42}Ca (95.9%)	^{42}Ca (95.9%)
TTY* ^{44gd}Sc (MBq/μAh)	630[(a)]	220	60(9)	44(7)	54[(d)]
TTY m/g % (exp)[(b)]	0.54	2.21	5.0(5)	10.9(1.4)	-
TTY m/g % (exp EXFOR)[(c)]	0.55	-	3.8	10.6	12.1
TTY m/g % (th)[(d)]	0.5	2.34	5.3	15.2	18.2

* Thick Target Yield
(a) Metallic target experimental data converted to $CaCO_3$
(b) From the thick target data
(c) From the experimental cross-sections and SRIM stopping powers
(d) Calculated using EMPIRE cross sections and SRIM stopping powers

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Distributed learning: predictive models based on data from multiple hospitals without data leaving the hospital

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Purpose: Personalized medicine is greatly facilitated by predictive models. In order to successfully train predictive models, large volumes of patient data are required. These data are readily available from hospitals worldwide, however, sharing these data is hampered by ethical, political, administrative and legal boundaries. A method by which these boundaries can be circumvented is distributed learning. In a distributed learning approach, the model application is sent to each individual hospital that contains data. The model learns from the data at the hospital. Subsequently, the models are sent back from the hospitals to a central location. At the central location, the models are combined to form a model that has been trained on all data.
In this work, we show that it is possible to train a Bayesian network using distributed learning on data from multiple

hospitals. The model predicts dyspnea, which is a common side effect of radiotherapy treatment of lung cancer.
Materials/methods: Clinical data from 229 lung cancer patients, treated with curative intent with chemoradiation (CRT) or radiotherapy (RT) alone were collected and stored in 5 different medical institutes (123 patients at Maastro (Netherlands, Dutch), 24 at Jessa (Netherlands, Dutch), 34 at Liege (Belgium, Dutch and French) and 48 at Aachen (Germany, German)). None of the patients received stereotactic body radiotherapy. Patients were treated for their primary lung tumor and had not had another tumor in the 5 years before treatment.
A Bayesian network model was trained on these data. Structure learning was done using the PC-algorithm at each hospital[1]. Network structures were transmitted to the central location, and using a voting algorithm, the optimal network structure was determined. Conditional probability tables were learned using the EM-learning algorithm[2]. Performance of the model was compared for a structure that was learned from multiple hospitals against a structure that was learned locally. The models were trained on data from Aachen, Liege and Jessa and validated on the data at Maastro. Performance was assessed using the area under curve (AUC) of the receiver operator characteristic. ROCs were compared using a method described by DeLong et al [3].
Results: The network structure of the globally learned Bayesian network can be observed in figure 1. The model performed above chance level for making predictions (AUC = 0.69, 95% CI: 0.58-0.80). The model that used a structure originating from local learning also performed above chance level (AUC = 0.67, 95% CI: 0.55-0.79). The globally learned structure allows the Bayesian network to perform marginally better (AUC of 0.69 vs 0.67), however, this improvement is not significant (p = 0.69).
Conclusions: In this work we show that it is possible to train a Bayesian network in a distributed setting, making a big stride forward to enabling personalized medicine in radiotherapy.

Keywords: Dyspnea, Bayesian networks, Distributed learning

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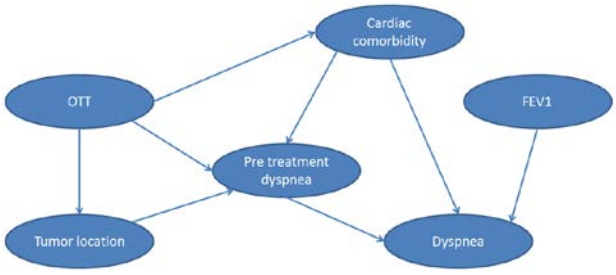

Figure 1: Network structure of the Bayesian network model. The Bayesian network uses, tumor location (right lower lobe, right middle lobe, right hilus, right upper lobe, left lower lobe, left upper lobe, left hilus, mediastinum), FEV1 (forced expiratory volume in 1 second, in %, adjusted for age and gender; measured prior to medication), pre-treatment dyspnea score (CTCAE grade < 2), baseline dyspnea score (CTCAE grade < 2), OTT (overall treatment time) and cardiac comorbidity (Non-hypertension cardiac disorder (at baseline)) to classify acute dyspnea.

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RSI: A genomic signature of radiosensitivity
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Most cancer patients receive radiation therapy (RT) during their illness. Virtually all RT courses are based on techniques and fractionation schemes determined by trial and error, often decades ago. Thus there is a pressing and urgent need for a molecular diagnostic to inform personalized RT delivery. Our team developed a molecular fingerprint of tumor radiosensitivity (RSI), and has subjected it to extensive clinical and analytical validation (1-5). RSI score distribution across disease sites is consistent with their known clinical radio-responsiveness as defined by the surviving fraction after 2 Gy (SF2), and has been validated in 2,200 patients in 12 independent datasets across several disease sites. We have shown that RSI correlates with outcome only in patients treated with RT; it is not prognostic but predictive. The National Cancer Institute designed the Clinical Assay Development Program (CADP) to assist with the development of assays that may predict therapy response or prognostic behavior of a diagnosed cancer; RSI has undergone further development through CADP.
Using RSI and the linear quadratic model, our team next modeled the genomically adjusted dose (GAD) to predict RT dose effect at the individual patient level. RSI/GAD has predicted cancer cohorts that will specifically benefit from RT-dose escalation, such as radioresistant luminal lesions in breast cancer (6) and some glioblastomas (7). Current data have also revealed that metastatic lesions have markedly different RSI than the primary lesion, which is further modified by the site of metastasis (8).
We will discuss current knowledge of RSI/GAD and describe ongoing current research plans to incorporate RSI, as a predictive biomarker of radiosensitivity, into personalized therapy options for RT patients.

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